

# BIOMATERIAL COMPRISING ADIPOSE-DERIVED STEM CELLS AND GELATIN AND METHOD FOR PRODUCING THE SAME

## FIELD OF INVENTION

**[0001]** The present invention relates to the field of stem cells and their use for the production of multi-dimensional biomaterials. In particular, the present invention relates to biomaterials comprising adipose-derived stem cells (ASCs), methods for preparing and using such biomaterials for therapy.

## BACKGROUND OF INVENTION

**[0002]** Tissue engineering involves the restoration of tissue structure or function through the use of living cells. The general process consists of cell isolation and proliferation, followed by a re-implantation procedure in which a scaffold material is used. Mesenchymal stem cells provide a good alternative to cells from mature tissue and have a number of advantages as a cell source for bone and cartilage tissue regeneration for example.

**[0003]** By definition, a stem cell is characterized by its ability to undergo self-renewal and its ability to undergo multilineage differentiation and form terminally differentiated cells. Ideally, a stem cell for regenerative medicinal applications should meet the following set of criteria: (i) should be found in abundant quantities (millions to billions of cells); (ii) can be collected and harvested by a minimally invasive procedure; (iii) can be differentiated along multiple cell lineage pathways in a reproducible manner; (iv) can be safely and effectively transplanted to either an autologous or allogeneic host.

**[0004]** Studies have demonstrated that stem cells have the capacity to differentiate into cells of mesodermal, endodermal and ectodermal origins. The plasticity of MSCs most often refers to the inherent ability retained within stem cells to cross lineage barriers and to adopt the phenotypic, biochemical and functional properties of cells unique to other tissues. Adult mesenchymal stem cells can be isolated from bone marrow and adipose tissue, for example.

**[0005]** Adipose-derived stem cells are multipotent and have profound regenerative capacities. The following terms have been used to identify the same adipose tissue cell population: Adipose-derived Stem/Stromal Cells (ASCs); Adipose Derived Adult Stem (ADAS) Cells, Adipose Derived Adult Stromal Cells, Adipose Derived Stromal Cells (ADSC), Adipose Stromal Cells (ASC), Adipose Mesenchymal Stem Cells (AdMSC), Lipoblasts, Pericytes, Pre-Adipocytes, Processed Lipoaspirate (PLA) Cells. The use of this diverse nomenclature has led to significant confusion in the literature. To address this issue, the International Fat Applied Technology Society reached a consensus to adopt the term "Adipose-derived Stem Cells" (ASCs) to identify the isolated, plastic-adherent, multipotent cell population.

**[0006]** Tissue reconstruction encompasses bone and cartilage reconstruction, but also dermis, epidermis and muscle reconstruction. Currently, each tissue defect should be treated with a specific treatment, requiring a different development for each.

**[0007]** There is thus still a need in the art for tissue engineered materials for tissue reconstruction and/or regeneration that are fully biocompatible and provide appropriate

mechanical features for the designated applications, although usable on a broad range of tissues. Therefore, the present invention relates to a graft made of ASCs differentiated in a multi-dimensional structure with gelatin.

## SUMMARY

**[0008]** The present invention relates to a biomaterial having a multi-dimensional structure comprising differentiated adipose-derived stem cells (ASCs), an extracellular matrix and gelatin.

**[0009]** In one embodiment, gelatin is porcine gelatin. In one embodiment, gelatin is in form of particles. In one embodiment, gelatin have a mean diameter ranging from about 50  $\mu\text{m}$  to about 1000  $\mu\text{m}$ , preferably from about 75  $\mu\text{m}$  to about 750  $\mu\text{m}$ , more preferably from about 100  $\mu\text{m}$  to about 500  $\mu\text{m}$ .

**[0010]** In one embodiment, the biomaterial is three-dimensional.

**[0011]** In certain embodiments, the biomaterial is moldable or formable.

**[0012]** In one embodiment, the ASCs are differentiated into cells selected from the group comprising or consisting of osteoblasts, chondrocytes, keratinocytes, myofibroblasts, endothelial cells and adipocytes.

**[0013]** The present invention also relates to a medical device or a pharmaceutical composition comprising the multi-dimensional biomaterial as described hereinabove.

**[0014]** Another aspect of the present invention is a method for producing the multi-dimensional biomaterial as described hereinabove comprising the steps of:

**[0015]** adipose-derived stem cells (ASCs) proliferation,

**[0016]** ASCs differentiation at the fourth passage, and

**[0017]** multi-dimensional induction, preferably 3D induction.

**[0018]** The present invention further relates to a multi-dimensional biomaterial obtainable by the method as described hereinabove.

**[0019]** Still another object of the present invention is a biomaterial as described hereinabove for use for treating a tissue defect. In one embodiment, the tissue is selected from the group comprising or consisting of bone, cartilage, dermis, epidermis, muscle, endothelium and adipose tissue.

## Definitions

**[0020]** In the present invention, the following terms have the following meanings:

**[0021]** The term "about" preceding a value means plus or less 10% of the value of said value.

**[0022]** The term "adipose tissue" refers to any fat tissue. The adipose tissue may be brown or white adipose tissue, derived from subcutaneous, omental/visceral, mammary, gonadal, or other adipose tissue site. Preferably, the adipose tissue is subcutaneous white adipose tissue. Such cells may comprise a primary cell culture or an immortalized cell line. The adipose tissue may be from any organism, living or deceased, having fat tissue. Preferably, the adipose tissue is animal, more preferably mammalian, most preferably the adipose tissue is human. A convenient source of adipose tissue is from liposuction surgery, however, the source of adipose tissue or the method of isolation of adipose tissue is not critical to the invention.